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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/701,887	11/04/2003	Steffen Nock	020144-002110US	6724

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EXAMINER	
KIM, YUNSOO	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/701,887	**Applicant(s)** NOCK ET AL.	
	Examiner Yunsoo Kim	**Art Unit** 1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 23 March 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: 25-27.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 11. does NOT place the application in condition for allowance because:

Claims 25-27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,099,005 (of record) in view of Kim et al. (Journal of Biol. Chem. 1994, vol. 269, pp. 12345-12350, of record), U.S. Pat. No. 6,358,710 (of record) and Pierce Product Information for ImmunoPure ®IgG1 Fab and F(ab')2 preparation kit (of record) and U.S. Pat. No. 4,281,061 (of record) for the reasons set forth in the office action mailed 12/19/06.

Applicants' arguments filed on 3/23/07 have been fully considered but they were not persuasive.

Applicants' traversed the rejection based on that the cited references failed to teach all limitations of the pending claims and it teaches away from the claimed invention.

Applicants argue that the '005 patent only teaches the method of enhancing immunoglobulin fragment yield. Kim et al. reference teaches observation of O-linked glycosylation. The '710 patent teaches merely a possible modification of general antibody's glycosylation status and the pierce product information provides protease composition but no enzyme for deglycosylation.

Contrary to applicants' arguments, the '005 patent teaches use of pepsin or papain treatment for production of F(ab)'2 fragments (col. 6, lines 34-40, in particular). In addition, the structural limitation of antibody having glycosylated antibody contains one or more non-hinge regions that are adjacent to the hinge region and have one or more attached oligosaccharide groups was taught by the Kim et al. reference (p. 12345, in particular). The hinge region of an antibody is located where the globular portions of the antibody joined by a flexible stretch of a polypeptide chain. As taught by Kim et al., the IgG molecules possess conserved glycosylation site at Asn-297 in the CH-2 (e.g. adjacent to hinge region) domain of heavy chains (see introduction, p. 12345, col. 1, in particular). Thus, the structural limitation of antibody having glycosylated antibody contains one or more non-hinge regions that are adjacent to the hinge region and have one or more attached oligosaccharide groups is an inherent property of the antibody.

In addition, the '710 patent is drawn to a humanized antibody and the teachings in col. 19-21 are specific for IgG anatibody (col. 19, lines 55-65, in particular) and the commercially available glycosidases (=deglycosylation enzyme, col. 20, lines 4-18, in particular). Even if the '710 patent only provides a general knowledge in the field of protein glycosylation, the ordinary skill in the art would have been motivated to extrapolate the deglycoslyation method in the protein field to deglycosylation of antibody using glycosydases especially when commercially available glycosidases are taught. Moreover, one cannot show non-obviousness by attacking the cited references individully where the rejection is based on the combinations of references (MPEP 2145(d)).

Therefore, it would have been obvious to one of the ordinary skill in the art at the time the invention was made to substitute the sialidase treatment prior to a protease treatment in a method of making F(ab)'2 fragment as taught by the '005 patent with a N-or O-glycosidases as taught by the Kim et al. and the '710 patent and package the glycosidase, proteases, purification medium and instruction into a kit format as taught by the Pierce Kit and the '061 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because Kim et al. teach the glycosylation renders the hinge region resistant against the proteolyses of the heavy chains and the '710 patent teaches that the N-linked or O-linked carbohydrates can be removed from the protein molecules by N-glycosidase or O-glycosidase, respectively to make more susceptible to protease treatment to enhance F(ab)'2 fragment production. It is well known in the art to assemble the active ingredients in a kit format as taught by the Pierce product information for convenience, optimization and economy of the users as taught by the '061 patent.

From the teachings of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Thus, the cited references teach all the limitations of the claimed invention and the combination of teachings remain obvious.

Yunsoo Kim
Patent Examiner
Technology Center 1600
April 18, 2007

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